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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
Maher M. Haddad	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 and 29-46* is/are pending in the application.

4a) Of the above claim(s) *29,32,34,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10, 30, 31, 33, 35-42 and 45-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)

5) ☐ Notice of Informal Patent Application (PTO-152)

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 03/08/04, is acknowledged.

2. Claims 10 and 29-46 are pending.

3. Claims 29, 32, 34 and 43-44 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 10, 30, 31, 33, 35-42 and 45-46 are under examination as as they read on an antibody which specifically binds to a polypeptide of SEQ IN NO: 1 and methods of making.

5. In view of the amendment filed on 03/08/04, only the following rejections are remained.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 35 and 38 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the same reasons set forth in the previous Office Action mailed 12/03/03.

A) The term "specificity" recited in claims 35 and 38, line 1 is ambiguous and unclear and the metes and bounds of the claimed "specificity" is not defined.

Applicant's arguments, filed 03/08/04, have been fully considered, but have not been found persuasive.

Applicant argues that the present claims meet the legal standards required by 35 U.S.C. 1 12, second paragraph because: i) Applicants submit that the term specificity was well understood by those skilled in the antibody arts at the time of the filing of the invention; and ii) Applicants have included scientific references in the specification explaining specificity, including references for assays to measure antibody specificity. (See the Specification, for example, at page 23, lines 26-34, and page 24, lines 9-36. Applicant concluded that claims 35 and 38, when read in light of the specification, reasonably apprise those skilled in the art of the scope of the invention and give fair notice of what constitutes infringement of those claims.

However, it is well known in the art that every antiserum has a different specificity because the repertoire of antibodies produced by animal is somewhat different. Thus, it is unclear one skill in the art would be able to make an antibody with the same specificity of the antibody to SEQ ID NO:1, variants or fragments thereof.

8. 35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

9. Claims 10, 30, 31, 33, 35-42 and 45-46 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the same reasons set forth in the previous Office Action mailed 12/03/03.

Applicant's arguments, filed 03/08/04, have been fully considered, but have not been found persuasive.

Applicant asserts that the antibodies have a variety of utilities, in particular in expression profiling, and for diagnosis of conditions or diseases characterized by expression of CDDZ, for toxicology testing, and for drug discovery (see the Specification, for example, at page 29, lines 20-27; and page 33, line 36 to page 37, line 10). Applicant draws the Examiner's attention to two expert Declarations under 37 C.F.R. 1.132 to support his position, and ten (10) scientific references filed before or shortly after the September 11, 1998 priority date of the instant application. Applicant contends that the Office Action does not dispute that the polynucleotides described in the subject application can be used as a probe in CDNA microarrays and used in gene expression monitoring applications and likewise, the use of antibodies which specifically bind to the polypeptides encoded by these polynucleotides in such applications.

This is not found persuasive. It is noted that toxicology testing and drug discovery are not specifically recited in the specification as originally filed. For utility to be "well established", it must be specific and substantial. The particulars of toxicology testing with SEQ ID NO: 1 are not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins, but is only potential with respect to SEQ ID NO: 1. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Furthermore, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form.

The Declaration by Dr. Vishwanath R. Iyer, filed 3/08/04, under 37 C.F.R 1.132 indicating that the use of microaary-based expression profiling to elucidate basic physiological responses, to study primary and secondary drug effects, or to discriminate and classify human cancers, expression profiling which relies for its power on comparison of patterns of expression. Dr. Iyer states that the resolution of the pattern used in such comparisons is determined by the number of genes detected: the greater the number of genes detected, the higher the resolution of the pattern. Dr. Iyer further states that each gene included as a probe on a microarray provides a signal that is specific to the cognate transcript, as least to a first approximation. Each new gene-specific probe

resolving power of the device. As an aside, the declaration does not address the issue at hand that is the utility of the antibody against SEQ ID NO: 1 rather than the nucleic acid probe. Regarding the merit of the argument, any new polynucleotide can be used in a microarray, and thus this asserted utility is not specific. The use of the any nucleic acid molecule as a probe to study primary and secondary drug effects or to discriminate and classify human cancers is not substantial utility in the absence of a disclosure of a specific DNA target as any DNA can be used as probe for DNA microarray-based expression profiling. Further, the use of the polynucleotide in an array to study primary and secondary drug effects or to discriminate and classify human cancers is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array.

The Declaration by Dr. John Coughlin Rockett, filed 3/08/04, under 37 C.F.R 1.132 indicating that as with nucleic acid microarrays, the greater the number of proteins detectable, the greater the power of the technique, the absence or failure of a protein to change in expression levels does not diminish the usefulness of the method, and prior knowledge of the biological function of the protein is not required. Further Dr. Rockett states that protein expression profiling is particularly useful to toxicologist, especially in the pharmaceutical industry. However, gene expression arrays operate under the pretense that changes in mRNA levels ultimately correlate to changes in encoded protein levels; often this assumption does not hold true. Additionally, gene expression arrays provide no information on protein post-translational modifications (phosphorylation, glycosylation, etc.) that affect cell function. Assign putative function to unknown sequences, and elucidate the biochemical basis of drug in a toxicological action have no "well-established" use for the polypeptide which the claimed antibody recognize. Moreover, use of the claimed polypeptide in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. This is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Appellant's individual polypeptides are affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polypeptides have no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this polypeptide could be put.

Applicant criticizes the examiner's position that the claimed polypeptides cannot be useful without precise knowledge of their biological function. However, Appellant is mischaracterizing the examiner's position. A specification can meet the legal requirements of utility and enablement for a new polypeptide which is recognized by the claimed antibody as long as the specification discloses a specific and substantial asserted utility for the new polypeptide, or a well-established utility for the claimed polypeptide. A hypothetical example may serve to

expressed in colon cancer and not expressed in healthy colon tissue. The hypothetical specification does not disclose the biological activity of the polypeptide. The claimed polypeptide in the hypothetical example would not be rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as it has utility and is enabled as a colon cancer marker. However, such is not the fact pattern here. The instant specification discloses that the claimed polypeptides are structurally related to *C. elegans* LIN-7 protein and hypothesizes that the claimed polypeptides are involved in disorders associated with defective cell signaling, including developmental disorders, such as Williams syndrome, oncogenesis and neuronal function (page 2, lines 27-35). However, the expression of the two polypeptides in diseased tissues and the corresponding healthy tissues was not evaluated. Therefore, there is no disclosure that the claimed polypeptides are expressed at altered levels or forms in any specific, diseased tissue relative to control healthy tissue. Significant further research would be required of the skilled artisan to identify such a disease or disorder and thus the asserted utility is not substantial.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 10, 30, 31, 33, 35-42 and 45-46 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention for the same reasons set forth in the previous Office Action mailed 12/03/03.

Applicant's arguments, filed 03/08/04, have been fully considered, but have not been found convincing.

Applicant argues regarding antibodies which specifically bind variants of SEQ ID NO: 1 that the skilled artisan could use the claimed antibodies to purify a protein having an amino acid sequence comprising a variant sequence of SEQ ID NO:1 (See the Specification, for example, at page 41, lines 24-34). In another use, antibodies to variants of the amino acid sequence of SEQ m NO: 1 can be used for drug screening purposes (See the Specification, for example, at page 33 line 36 to page 34 line 14). Additionally, antibodies which specifically bind to variants of SEQ ID NO:1 can be used, for example, in 2D-PAGE analysis for expression profiling related to toxicology testing, drug discovery and disease diagnosis.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the claimed antibody which specifically binds to the polypeptide of SEQ ID NO: 1 has no use, see above.

Applicant argues that claim 10 recites not only that the variant polypeptides are at least 90% identical to SEQ m NO:1, but also have "**a naturally-occurring amino acid sequence**." through the process of natural selection, nature will have determined the appropriate amino acid sequences. Applicant argues that given the information provided by SEQ ID NO:1 encoded by SEQ ID NO:2, one of skill in the art would be able to routinely obtain "a naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" by performing hybridization and/or PCR techniques.

However, in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and/or use the invention, not how to screen by performing hybridization and/or PCR techniques to identify the invention. Until the time when the at least 90% sequence identity polypeptides are found, then one skill in the art can make them.

Applicant criticizes Coleman et al., Abaza et al., Lederman et al., and Li et al., as these references are not relevant to the case at hand. Applicant contends that the mutations were "artificially" in these cases were created in the laboratory and, therefore, are not analogous to molecular evolution, which is profoundly influenced by natural selection. For example, the deactivating mutations as described by these references would almost certainly not be tolerated in nature. Furthermore, it is clear that over the course of evolution, amino acid residues that are critical for protein function are conserved. Applicant concludes that the amino acid differences are likely to represent substitutions that do not alter protein function.

Contrary to Applicants' assertions, Lederman *et al*, teach a correlation between the genetic structure and the phenotype of the encoded protein in relation to the binding of mAbs, for example a common African allele of CD4, which is considered to be a naturally occurring event, has been identified by non-reactivity with the monoclonal antibody, OKT4. Lederman *et al*, further teaches that an arginin→ tryptophan substitution at amino acid 240 relative to $CD4^{OKT+}$ is found in chimpanzee, rhesus macaque, mouse and rat CD4 suggesting that this mutation may confer unique functional properties to the $CD4^{OKT4-}$ protein. Therefore, Lederman *et al* demonstrated that even a single amino acid change can ablate binding of the monoclonal antibody. Furthermore, Colman *et al* teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Colman *et al* provide an example of escape mutants of viral antigens which were selected by growth of virus in the presence of monoclonal antibody (natural selection), provide many examples of the type of substitution which can render the antigen unrecognizable by the selection antibody. These references demonstrate that event a single amino acid substitution or what appears to be an inconsequential chemical modification can ablate binding of the antibody.

Applicants argue that Ngo *et al* reference cited by the Examiner relating to structure-antigenicity relationships in proteins is simply not germane to whether one can make and use the polypeptide variants recited by the present claims regardless of the function of the SEQ ID NO:1 variants , one can make those polypeptide variants using the disclosure. Applicants further bring to the

identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. Contrary to Applicant's assertions, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 1 is essential for maintain its functional activity and which changes can be made in the structure of SEQ ID NO: 1 and still maintained the same function. The new fold structures for which there is no functional information represents a problem that it may be impossible to infer function. Further a medium range overall sequence similarity is not enough to conclude that two proteins would have the same function. For instance, many proteins that are transmembrane proteins will have similar structural regions in the membrane spanning domains, but differ in their catalytic domains, etc... Only experimental evidence can confirm the scientist best guess of a computer-based modeling. Furthermore, it is known that certain specific conserved sequences are responsible for the actual structure of the protein. Mutations in the conserved patterns without much change in the overall sequence would lead to a change in the essential active site structure and therefore to a change in function. Such mutations could lead to the formation of proteins with high sequence homology but different functions. Of course, the mutant protein will be retained in nature only if serves some useful purpose.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention with the different antibodies as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (*In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

12. Claims 10, 30, 31, 33, 35-42 and 46 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 12/03/03.

Applicant's arguments, filed 03/08/04, have been fully considered but not persuasive.

A. The Specification provides an adequate written description of the claimed antibodies which specifically bind to the recited "variants" of SEQ m NO:1.

Applicant contends that given any naturally occurring polypeptide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO: 1. Applicant concludes that the specification provides an adequate written description of the recited polypeptide variants of SEQ ID NO:1.

However, to satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would

F.3d at 1563. The written-description requirement can be satisfied "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572. As for the recitation of "naturally-occurring polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1". The court said that " an adequate written description of a DNA ... 'requires a precise definition, such as by structure, formula, chemical name, or physical properties.' Not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566 (quoting *Fiers*, 984 F.2d at 1171). The Specification, fails to provide working examples of any variants. Furthermore, the specification fails to satisfy the written-description requirement because the specification does not disclose direction as what is the use of the claimed polypeptide. The specification only discloses SEQ ID NO: 1, none of the variants were provided, nor is there any guidance as to which should be used. The court stated that "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, what is required is a description of the DNA itself." *Fiers* 984 F.2d at 1170.

1. The present claims allegedly define the claimed genus through the recitation of chemical structure.

Applicant asserts that the antibody claims in the instant application define SEQ ID NO: 1 in terms of chemical structure rather than in terms of functional characteristics. Applicant contends that in *Lilly* and *Fiers*, the nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement. In contrast, Applicant argues that the instant claims define the polypeptides bound by the claimed antibodies in terms of chemical structure, rather thatn functional characteristics. Applicant concludes that the instant claims are fundamentally different from those found invalid in *Lilly* and *Fiers*.

Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polypeptide recited in the claims. The description of one CJPDZ polypeptide of SEQ ID NO:1 in the specification of the instant application is not a representative number of embodiments to support the description of an entire genus of functionally equivalent polypeptides which incorporate all mutants, derivatives, variants and fragments having at least 90% identity to the amino acid sequences of SEQ ID NO: 1. Therefore, only an isolated polypeptide of sequence of SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Further, the "naturally occurring" language in the claims is analogous to the claims found in *Lilly* and *Fiers* because the claimed polypeptides are defined only by their homology to SEQ ID NO:1, which is insufficient to satisfy 112(1) since "a mere wish or plan" for obtaining an up to 10% variation in SEQ ID NO: 1 is not enough to comply with 112(1). Furthermore, there is no described or art-recognized correlation or relationship between the structure of the invention, the CJPDZ protein and it's function, the feature deemed essential to the instant invention. Therefore, one of skill in

2. The present claims do not define a genus which is "highly variant".

Applicant asserts that the claims at issue do not describe a genus which could be characterized as "highly variant", but rather a genus that is narrow in scope. Applicant directed Examiner's attention to Brenner et al reference to demonstrate that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned for establishing evolutionary homology between two sequences aligned over at least 150 residues. Appellant concluded base on Brenner et al reference teachings that the claimed antibodies to the cell junction PDZ protein of SEQ ID NO: 1 that naturally occurring molecules may exist which could be characterized as CJPDZ proteins and which have as little as 30% identity over at least 150 residues to SEQ ID NO:1. Applicant states that the variant language of the present claims recites, for example, polypeptides comprising "a naturally-occurring human amino acid sequence having at least 90% identity to the sequence of SEQ ID NO: 1 (SEQ ID NO: 1 has 233 amino acids). Applicant argues that this variation is far less than that of all potential CJPDZ proteins related to SEQ ID NO: 1. As discussed above, Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polypeptides recited in the claims. The specification and claims do not indicate what characteristics are shared by members of the genus. The scope of the claims include numerous structural variants and the genus is highly variant because a significant number of structural differences between genus members is permitted. However, the specification and claims do not provide any guidance as to what changes should be made and structural features that distinguish polypeptides in the same genus from others in the protein class are absent from the specification. The specification fails to disclose the common characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 1 are insufficient to describe the genus.

3. The state of the art at the time of the present invention is allegedly further advanced than at the time of the *Lilly* and *Fiers* applications.

Applicant contends that much has happened in the development of recombinant DNA technology in the 20 or more years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. Appellant indicates that, for example, PCR, highly efficient cloning and DNA sequencing technology has been developed. Appellant asserts that with the current advances, one of skill in the art would recognize that, given the sequence information of SEQ ID NO: 1 and the additional extensive detail provided by the application, the present inventors were in possession of the polypeptide variants recited by the claims at the time of filing of this application.

Appellant's arguments have been considered but are not found to be persuasive because the broad brush discussion of making and screening for allelic variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the polypeptides CJPDZ of SEQ ID NO: 1 is disclosed. The specification's

Further, in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and use the invention, not how to identify the invention. Until the time when at least 90% sequence identity to the claimed polypeptide are found, then one skill in the art can make them. Undue experimentation would be required of the skilled artisan to obtain "naturally occurring" CJPDZ variants and determine their specific activity.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 35-40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent. No. 6,051,374 (of record) in view of U.S. Patent No. 6,210,675 (of record) for the same reasons set forth in the previous Office Action mailed 12/03/03.

15. Claims 10, 36, 39, 41, 42 and 45-46 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset et al (GenBank Accession No. AF028826, Nov.1997), as is evidenced by Rousset et al (Oncogene16:643-654, 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost et al. (Immunol. Invest. 1988; 17:577-586) for the same reasons set forth in the previous Office Action mailed 12/03/03.

16. Claims 10, 36, 39, 41, 42 and 45-46 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset et al (Oncogene16:643-654, Feb 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost et al. (Immunol. Invest. 1988; 17:577-586) for the same reasons set forth in the previous Office Action mailed 12/03/03.

17. Claims 35-36 and 38-39 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset et al (GenBank Accession No. AF028826, Nov.1997), as is evidenced by Rousset et al (Oncogene16:643-654, 1998) in view of Alisa Campbell (General properties and applications of

et al. (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of Harlow (1989) for the same reasons set forth in the previous Office Action mailed 12/03/03.

18. Claims 35-36 and 38-39 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset et al (Oncogene16:643-654, Feb 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost et al. (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of Harlow (1989) for the same reasons set forth in the previous Office Action mailed 12/03/03.

19. Claim 30 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset et al (GenBank Accession No. AF028826, Nov.1997), as is evidenced by Rousset et al (Oncogene16:643-654, 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost et al. (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of Owens et al (1994) (of record) for the same reasons set forth in the previous Office Action mailed 12/03/03.

20. Claim 30 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset et al (Oncogene16:643-654, Feb 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost et al. (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of Owens et al (1994) (of record) for the same reasons set forth in the previous Office Action mailed 12/03/03.

21. Claim 31, 33, 37, and 40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset et al (GenBank Accession No. AF028826, Nov.1997), as is evidenced by Rousset et al (Oncogene16:643-654, 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost et al. (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of U.S. Patent No. 6,210,675 for the same reasons set forth in the previous Office Action mailed 12/03/03.

22. Claims 31, 33, 37, and 40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Rousset et al (Oncogene16:643-654, Feb 1998) in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1), as is evidanced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586), as applied to claims 10, 36, 39, 41, 42 and 45-46 above, and further in view of U.S. Patent No. 6,210,675 for the same reasons set forth in the previous Office Action mailed 12/03/03.

Applicant's arguments, filed 03/08/04, have been fully considered but not persuasive.

Applicant acknowledges that the peptides of the '374 patent and Rousset *et al* each recognizably share regions of sequence identity with Applicant's protein.

Applicant argues that irrespective of this identity, antibodies that "specifically binds" with the peptide of either the '374 patent and Rousset *et al.* would not "specifically binds" with the protein of instant SEQ ID NO:1. Applicant argues that in order for an antibody to specifically bind to a polypeptide comprising the amino acid of SEQ ID NO: 1 or a "90% variant" of SEQ ID NO: 1, one muse have the sequence information of SEQ ID NO: 1. Applicant further asserts that any antibody that bound both the instant protein and either prior art protein would do so by "cross-reacting", and that an antibody cannot be both specific for the instant protein and cross-react with related proteins.

However, Applicant's argument attempts to limit the term "specifically binds" in a manner inconsistent with the well-known and art-recognized specificity of antibody interaction with epitopes defined by particular amino acid sequences. That an antibody "cross-reacts", i.e., binds to more than one protein sequence, does not mean that the antibody does not "specifically react" with both proteins. (see Bost et al evidentiary reference.). Consequently, it was well known in the art at the time the invention was made that antibody binding of distinct proteins was indeed specific.

23. No claim is allowed.

24. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

225. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

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April 30, 2004

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